Syncope in Adults: Terminology, Classification, and Diagnostic Strategy

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Syncope is a relatively common clinical syndrome that is a subset of a broader range of conditions that cause transient loss of consciousness (TLOC). Other TLOC conditions include seizures, concussions, and intoxications. However, despite frequent confusion in the medical literature, syncope is and should be clearly distinguished from those other causes of TLOC by virtue of its pathophysiology; specifically, syncope is the result of self-terminating inadequacy of global cerebral nutrient perfusion, while the other forms of TLOC have different etiologies. Unfortunately, the diagnostic evaluation of syncope remains for the most part poorly managed and inefficient. Careful history-taking, physical examination, and judicious use of tests can not only increase the diagnostic yield of the evaluation, but also increase patient safety and reduced overall healthcare costs. (PACE 2006; 29:1160–1169)

**Introduction**

Syncope is a clinical syndrome that is best thought of as being a subset of a broader range of conditions that cause transient loss of consciousness (TLOC). Other non-syncope TLOC conditions include seizures, concussions, and intoxications.

The aim of this communication is to provide a brief update regarding syncope terminology and classification, and a succinct assessment of its principal causes and evaluation strategies. However, it must be acknowledged that for many recommendations, suitable controlled trials are not available and substantial differences of opinion remain among knowledgeable practitioners.

**Pathophysiology**

A comprehensive review of the pathophysiology lies outside the scope of this communication; the interested reader is referred to references 1–3. In essence, however, it is the pathophysiology of syncope that distinguishes it from other causes of TLOC: specifically, syncope is the result of self-terminating inadequacy of global cerebral nutrient perfusion. Other forms of TLOC have quite different mechanisms. Thus, syncope is most often the result of transient systemic hypotension; on rare occasions, however, it may be triggered by acute global cerebral oxygen deprivation of other cause (e.g., abrupt loss of oxygen at high altitude). In contrast, seizures are a primary electrical disturbance of brain function, while concussion is obviously a disturbance of traumatic origin, and intoxications arise as the result of ingested (most often) agents.

**Ongoing Problems with Terminology**

Syncope accounts for approximately 1% of Emergency Room visits, and is the sixth most common cause of hospital admissions for patients over 65 years. The economic impact on healthcare costs alone is substantial. However, despite the fact that syncope is such a frequent clinical problem, its evaluation is for the most part poorly managed and inefficient. In part, this ineffectiveness is due to a lack of clarity as to what “syncope” is; the result is inclusion of “non-syncope” conditions such as seizures and concussions that unnecessarily confound physicians’ concept of the appropriate “syncope” evaluation, and result in their undertaking expensive but low-yield tests such as electroencephalograms (EEGs) and imaging studies of the head.

Unfortunately, despite the efforts of some, the terminology confusion continues to be exacerbated by imprecision in several recent prominent publications. For example, a recent important scientific statement from the American College of Cardiology Foundation, and the American Heart Association (AHA) confuses the definition of “true syncope” with the broader concept of TLOC; the impact of this error is evidenced, for example, by the inclusion of seizure disorders in the statement without pointing out the crucial distinction between seizures and syncope. A similarly imprecise characterization of syncope is found in a widely cited report from the Framingham study; in this case, “neurological” conditions (including seizure...
SYNCOPE DIAGNOSIS

disorders) are considered a cause of “syncope.” Finally, a relatively recent clinical review article in the British Medical Journal, in which both “neurological” and “psychiatric” causes are purported to be important causes of syncope, only serves to further confuse readers. Ultimately, promulgating misconceptions such as these muddies the water, is detrimental to advancing care, and does not speak well of the quality of the medical advice being offered.

Despite the persistence of unclear thinking in the literature, an effort has been made to both address the vagaries of terminology, Most importantly, the European Society of Cardiology (ESC) Syncope Task Force has formulated comprehensive guidelines for optimizing care of syncope patients. These guidelines not only clearly define the problem and highlight how syncope differs from other forms of TLOC, but also provide direction regarding the most effective evaluation and treatment strategies, including advocacy of the development of multidisciplinary Syncope Management Units (SMU) in order to facilitate care. In support of this latter concept, one recent study found that a more systematic approach to syncope such as that proposed by the ESC guidelines led to fewer hospitalizations, fewer lab tests, and higher rate of diagnosis.

TLOC: Syncope Versus Non-Syncope

At the outset, in the evaluation of patients who may have experienced a loss of consciousness spell, it is crucial to distinguish between disorders that may cause “true” TLOC, and ones that do not. In this regard, the meaning of consciousness merits attention.

From neuroscience and psychiatry perspectives, “consciousness” is considered to have both “arousal” and “content” aspects. The “arousal” aspect concerns the individual’s “responsiveness,” ranging from being categorized as “fully alert,” through a state of diminished attention, to stupor, to obtunded, to coma. The “content” feature concerns aspects such as self-awareness. Complex partial seizures are an example of a state in which the content of consciousness is impaired, but in which patients are still upright and look awake. However, for most physicians concerned with the TLOC evaluation, the assessment of “unconsciousness” focuses on loss of the arousal aspect only. Thus, in this view, a “true” TLOC patient may seem to be asleep but is not immediately arousable. Circumstances in which the patient appears to be awake, but the “content” of thought is perhaps questionable, may be of importance in the neurological or psychiatric evaluation of patients, but is less relevant in the context of this discussion.

With this definition of “consciousness” in mind, a number of patients may present with circumstances in which they seemed to have suffered a TLOC spell, but in fact they have not. Indeed, if the medical history and eyewitness reports are carefully assessed, the patient may never have lost consciousness at all. Conditions that mimic TLOC include cataplexy, drop attacks, psychogenic pseudo-syncope, and on some occasions, simple “falls.” Certain of these conditions (e.g., cataplexy, psychogenic pseudo-syncope) may reasonably be considered to be syndromes of transient abnormal responsiveness, but are not TLOC (and therefore are not syncope).

Once it has been established that TLOC has actually occurred (again based on detailed evaluation of the medical history and eyewitness accounts), the clinician must differentiate between syncopal and non-syncopal causes of TLOC. As alluded to earlier, errors abound in the medical literature in this regard, and the reader is referred to the ESC guidelines for comprehensive treatment of the issue. Only those circumstances in which loss of consciousness can reasonably be attributed to transient cerebral hypoperfusion should be considered “syncope.”

Syncope Classifications

- **Neurally-Mediated**
  - VVS = vasovagal syncope
  - CSS = carotid sinus syndrome

- **Orthostatic**
  - Autonomic Failure
  - Drug Effects
  - Volume Depletion

- **Cardiac Arrhythmias**

- **Structural Cardiopulmonary Disease**

- **Cerebrovascular**
  - Vascular Steal

Figure 1. A classification of the causes of syncope (some examples are indicated, but see text for additional details). VVS = vasovagal syncope; CSS = carotid sinus syndrome.
Causes of Syncope: A Diagnostic Classification

Establishing the cause or causes of syncope serves two principal purposes. First, an etiologic diagnosis permits assessment of prognosis and risk of recurrence, both issues of great concern for patients. Second, identifying the causes is the only way to provide with confidence a treatment recommendation aimed at both preventing recurrences and avoiding injury or death.

Determining the most probable causes of syncope in individual patients is often a challenging task, but one that is facilitated by considering the possible etiologies in an organized manner. To this end, the ESC Syncope Task Force1 recommended using a classification scheme similar to the one presented in Figure 1, beginning with the most frequently encountered conditions, the neurally mediated reflex faints. However, even after a thorough assessment, it may not be possible to assign a single cause for fainting. Often, patients have multiple co-morbidities and as a consequence they may have several equally probable causes of fainting. The physician must not assume too readily that an observed “abnormality” is either the certain cause or the sole cause of fainting in a given individual.19

Neurally mediated reflex faints are of several different types, but the best known is the common or vasovagal faint. The vasovagal faint can occur in both healthy persons as well as those with health problems; it is not indicative of nervous system disease and should not typically initiate neurological studies. The patient experiencing a vasovagal type of reflex faint is very likely to feel nauseated and sweaty before fainting, and often appears pale and feels clammy. After the fact, they often feel tired; this sensation may last hours or days. Other neurally mediated reflex faints include carotid sinus syndrome, and situational faints such as those that may be triggered by blood draws, emotional upset, pain, micturition, defecation, coughing, or swallowing.

Orthostatic (postural) hypotensive faints are as common or perhaps even more common than vasovagal syncope. Orthostatic faints are most often associated with movement from lying or sitting to a standing position. Apparently healthy individuals may experience minor symptoms (“light-headedness,” “greying-out”) as they stand up if blood pressure is slow to respond to the stress of upright posture. If the blood pressure is not adequately maintained during standing, faints may develop. However, the resulting “transient orthostatic hypotension” does not necessarily signal any serious underlying disease. The most susceptible individuals are elderly frail individuals, or persons who are dehydrated from hot environments or inadequate fluid intake. More serious orthostatic hypotension is often the result of certain commonly prescribed medications such as diuretics, β-adrenergic blockers, other anti-hypertensives (including vasodilators), and nitroglycerin. In a small percentage of cases, the cause of orthostatic hypotensive faints is structural damage to the autonomic nervous system due to systemic diseases (e.g., amyloidosis or diabetes) or in neurological diseases (e.g., Parkinson’s disease).

Cardiac arrhythmias may cause faints if the heart rate is excessively rapid or too slow. Such faints occur in healthy people at the onset of a paroxysmal supraventricular tachycardia (SVT). However, individuals with underlying heart disease are at greater risk. In either case, the faint tends to occur at the onset of the rhythm problem, but may also occur when a rapid abnormal rhythm stops suddenly, and a pause ensues before the normal heart rhythm takes over again.

Structural cardiopulmonary diseases are relatively infrequent causes of faints. The most common cause in this category is fainting associated with an acute myocardial infarction or ischemic event. The faint in this case is primarily caused by an abnormal nervous system reaction similar to the reflex faints. In general, faints caused by structural disease of the heart or blood vessels are particularly important to recognize, as they are warning of potentially life-threatening conditions. Among other conditions prone to trigger syncope (by either hemodynamic compromise or by a neural reflex mechanism, or both), some of the most important are hypertrophic cardiomyopathy, acute aortic dissection, pericardial tamponade, pulmonary embolism, aortic stenosis, and pulmonary hypertension.

Cerebrovascular disease is rarely the cause of a faint. Perhaps, subclavian steal is the best example in this class, but it is extremely uncommon. Loss of consciousness may occur during a verteobasilar transient ischemic attack (TIA), but not without accompanying evidence of brainstem dysfunction, such as cranial nerve deficits (e.g., diplopia, swallowing difficulties, dysarthria), paresis, or ataxia. Their absence during a spell of unconsciousness virtually rules out TIAs as a cause.

Certain clinical presentations that are clearly not syncope are often mislabeled as “syncope,” even in seemingly authoritative publications.9–11 As a consequence of this confusion (often aggravated by the manner in which even well-known investigators present their findings in the literature), the diagnostic process needed to arrive at the correct etiologic cause of an apparent TLOC spell is impaired. The most common conditions in this category include: seizures, sleep disturbances,
accidental falls, and some psychiatric conditions (e.g., anxiety attacks, severe hyperventilation, and hysterical reactions). Sleep disturbances can also be mistaken for TLOC. Inner ear problems causing dizziness (vertigo) are also frequently mislabeled as faints despite the absence of TLOC. Neurological and metabolic disturbances (such as hypoglycemia in diabetes) are only very rarely the cause of true fainting.

Initial Evaluation of the Patient with Suspected Syncope

Excluding any need for emergency medical attention to deal with physical injury, the initial medical evaluation of individuals suspected of having suffered a syncope spell begins with careful medical history-taking (focusing on the details of the apparent loss of consciousness event or events), a physical exam (including supine and upright BP), an electrocardiogram (ECG), and often an echocardiogram (in order to determine convincingly whether or not structural heart disease is present)\(^1\) (Fig. 2).

The medical history-taking is by far the most important part of this initial evaluation.\(^1\),\(^2\),\(^20\)–\(^25\) However, before beginning, it is essential to determine whether the patient can be relied upon to provide an accurate account of events. Many fainters, particularly the elderly, lack detailed recall of the event(s). Others may exhibit cognitive impairment that diminishes the diagnostic value of the medical history. Yet others may prove unreliable historians if there is potential risk to vocation, avocation, or driving privilege. In any event, it is crucial that family members and witnesses should be interviewed as part of the history-taking process.

From a practical perspective, in order to characterize the patient’s symptoms, it is helpful to have the patient focus first on the most recent TLOC event. After a thorough description is obtained, the next most recent episode should be assessed. Witnesses are an essential source of detail, filling in items that the patient may not recall. Table I provides insight into clinical features and their relationship to possible underlying causes of the faints.

In many patients, multiple causes may be responsible for TLOC symptoms. These may be identified or at least suggested by the medical history. In particular, clinicians should pay careful attention to the presence of co-morbidities. Co-morbidities may act synergistically (e.g., diabetic neuropathy and drug-induced orthostasis), or they may act independently, thereby resulting in more than one “cause” for the faint.

The history-taking process for syncope patients has been the subject of recent quantitative analysis. In a study of 80 syncopal patients with neurally mediated syncope, atrioventricular (AV) block, or ventricular tachycardia, Calkins et al. compared clinical histories to determine features predictive of each cause of syncope.\(^20\) A standard questionnaire was used. The historical features of syncope due to ventricular tachycardia and AV block were similar and differed from those of patients with neurally mediated syncope. Loss of consciousness due to ventricular tachycardia was associated with male gender, age > 54 years, \(\leq 2\) episodes of syncope, and a duration of warning.

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**Figure 2.** Depiction of a strategy for evaluation of patients with suspected syncope. The initial evaluation step is indicated at the top (see text for details). Thereafter, subsequent steps depend on whether the “initial evaluation” has provided a “certain” cause, or whether the cause remains “suspected” or “unexplained.” The scheme is adapted from the work of the ESC Syncope Task Force.\(^1\) PE = physical examination; BP = blood pressure; Echo = echocardiogram; NMS = neurally mediated syncope; OH = orthostatic hypotension.
### Table I.
Diagnosis From the Medical History in TLOC

#### A. Prior to the Attack

<table>
<thead>
<tr>
<th>Posture</th>
<th>Reflex syncope and autonomic failure less likely, otherwise all possible causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lying</td>
<td></td>
</tr>
<tr>
<td>Standing</td>
<td>Autonomic failure (in that case occurrence related to duration of standing), otherwise all possible causes</td>
</tr>
</tbody>
</table>

#### Activity

<table>
<thead>
<tr>
<th>Standing or after standing up</th>
<th>Autonomic failure (in that case occurrence related to duration of standing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Micturition, defecation</td>
<td>Reflex syncope</td>
</tr>
<tr>
<td>Protracted coughing</td>
<td>Reflex syncope</td>
</tr>
<tr>
<td>Swallowing</td>
<td>Reflex syncope including carotid sinus hypersensitivity</td>
</tr>
</tbody>
</table>

#### Predisposing factors

<table>
<thead>
<tr>
<th>After a meal</th>
<th>Autonomic failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head movements, pressure on the neck, shaving</td>
<td>Carotid sinus hypersensitivity</td>
</tr>
<tr>
<td>Fear, pain, stress</td>
<td>Reflex syncope (classic vasovagal variant: “common faint”)</td>
</tr>
<tr>
<td>During physical exercise</td>
<td>Cardiac: structural cardiopulmonary disease</td>
</tr>
<tr>
<td>Directly after cessation of physical exercise</td>
<td>Autonomic failure</td>
</tr>
<tr>
<td>During exercise of the arms</td>
<td>Steal syndrome</td>
</tr>
<tr>
<td>Palpitations</td>
<td>Cardiac: arrhythmia</td>
</tr>
<tr>
<td>Startling (e.g., alarm clock)</td>
<td>Prolonged QT syndrome</td>
</tr>
<tr>
<td>Seeing flashing light</td>
<td>Epilepsy with photosensitivity</td>
</tr>
<tr>
<td>Sleep deprivation</td>
<td>Epilepsy</td>
</tr>
<tr>
<td>Heat</td>
<td>Reflex syncope, autonomic failure</td>
</tr>
</tbody>
</table>

#### B. At the Onset of the Attack

| Nausea, sweating, pallor | “Autonomic activation”: reflex syncope |
| Pain in shoulders, neck (“coathanger pattern”) | Ischemia of local muscles: autonomic failure |
| Rising sensation from abdomen, unpleasant smell or taste, or other phenomena specific to subject but recurring over attacks | Epileptic aura |

#### C. During the Attack (Eyewitness Account)

<table>
<thead>
<tr>
<th>Fall</th>
<th>Tonic phase epilepsy, rarely syncope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keeling over, stiff</td>
<td>Syncope (all variants)</td>
</tr>
</tbody>
</table>

#### Movements*

| Beginning before the fall | Epilepsy |
| Beginning after the fall | Epilepsy, syncope |
| Symmetric, synchronous   | Epilepsy |
| Asymmetric, asynchronous | Epilepsy, may be epilepsy |
| Beginning at onset unconsciousness | Epilepsy |
| Beginning after onset unconsciousness | Syncope |
| Lasting less than about 15 seconds | Syncope more likely than epilepsy |
| Lasting for minutes      | Epilepsy |
| Restricted to one limb or one side | Epilepsy |

#### Other aspects

| Automatisms (chewing, smacking, blinking) | Epilepsy |
| Cyanotic face                          | Epilepsy |
| Eyes open                              | Epilepsy as likely as syncope |
| Tongue bitten                          | Epilepsy |
| Incontinence                           | Epilepsy as likely as syncope |

*continued.*
Table I. Continued

<table>
<thead>
<tr>
<th>D. After the Attack</th>
<th>E. Antecedent Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea, sweating, pallor</td>
<td>Recent start or change of medication</td>
</tr>
<tr>
<td>Clearheaded immediately on regaining consciousness</td>
<td>History of heart disease</td>
</tr>
<tr>
<td>Confused during minutes after regaining consciousness</td>
<td>Parkinsonism</td>
</tr>
<tr>
<td>Aching muscles (not to be confused with local bruises)</td>
<td>History of epilepsy</td>
</tr>
<tr>
<td>Prolonged fatigue</td>
<td>Psychiatric history</td>
</tr>
<tr>
<td></td>
<td>Occurrence of sudden death in family members</td>
</tr>
<tr>
<td></td>
<td>Metabolic disorders (e.g., diabetes)</td>
</tr>
<tr>
<td></td>
<td>Use of medication (anti-hypertensives, anti-angina,</td>
</tr>
<tr>
<td></td>
<td>anti-depressives, phenothiazines, anti-arrhythmics,</td>
</tr>
<tr>
<td></td>
<td>diuretics)</td>
</tr>
</tbody>
</table>

| “Autonomic activation”: syncope                                                    | Autonomic failure, may be arrhythmia                        |
| Syncope, may occur in epilepsy                                                    | Cardiac: arrhythmia or structural cardiac disease           |
| Epilepsy                                                                           | Autonomic failure (primary type)                             |
| Epilepsy                                                                           | Epilepsy                                                    |
| Reflex syncope                                                                     | Epilepsy                                                    |
|                                                                                  | May be psychogenic, but remember to check for autonomic     |
|                                                                                  | failure due to medication!                                  |
|                                                                                  | Arrhythmia, specifically prolonged QT syndrome              |
|                                                                                  | Real, non-circulatory transient loss of consciousness or    |
|                                                                                  | autonomic failure (secondary)                               |
|                                                                                  | Autonomic failure due to medication, hypovolemia, arrhythmia |

≤5 seconds. In contrast, palpitations, blurred vision, nausea, warmth, diaphoresis, or lightheadedness prior to syncope; and nausea, warmth, diaphoresis, or fatigue following syncope, were more predictive of neurally mediated syncope than of other forms. The combination of four factors could predict the cause of syncope with 98% sensitivity and 100% specificity.

Alboni et al. evaluated 341 patients with causes of syncope established by standardized diagnostic criteria, including cardiac and neurally mediated reflex syncope.21 A standard questionnaire was again used, focusing on the historical findings surrounding the syncope. Heart disease independently predicted a cardiac cause of syncope with 95% sensitivity and 45% specificity. Absence of heart disease excluded cardiac syncope in 97% of patients. In the presence of known or suspected heart disease, the most specific predictors of cardiac syncope were loss of consciousness while supine or during effort. The most important predictors of neurally mediated syncope were time between the first and the most recent episode ≥4 years, abdominal discomfort before syncope, and nausea and sweating. In patients without heart disease, the only significant finding suggestive of a cardiac cause was palpitations prior to syncope.

The most comprehensive evaluation to date examining the value of historical diagnostic elements in the assessment of TLOC has been provided by Sheldon et al.23,24 In the first of these reports,23 a uniform history questionnaire was completed by 671 TLOC patients. Patients with clearcut diagnoses based upon conventionally accepted criteria, were tested first. Their responses were analyzed to identify the historical features that most accurately correlated with their diagnoses. Thereafter, the findings were used to address the clinically most disconcerting issue, namely, whether it was possible to differentiate between epileptic seizures and syncope. To this end, the findings were tested in 539 TLOC patients, including individuals with complex partial epilepsy, primary generalized epilepsy, vasovagal syncope, ventricular tachycardia, heart block, and SVTs. The point score based on symptoms alone correctly classified 94% of patients, diagnosing seizures with 94% sensitivity and 94% specificity. Therefore, a simple point score of historical features may help to distinguish syncope from seizures with very high sensitivity and specificity. Nevertheless, it would be prudent at this stage to rely upon such methods only as a “screening” tool, and request expert consultation before coming to a definitive diagnosis (especially if the patient is to be labeled as having epilepsy).

In summary, a thorough initial evaluation (and in particular, meticulous history-taking by an experienced practitioner) often permits establishing a diagnosis, albeit necessarily a tentative one in
many cases. Questionnaires developed for the purpose may be of additional benefit and likely will become more widely utilized. In essence, depending on the physician’s comfort with the initial diagnosis (a state-of-affairs often heavily influenced by experience), patients can be classified as having a certain diagnosis, a suspected diagnosis, or no diagnosis (unexplained syncope). Figure 2 depicts the evaluation to this stage, and provides direction regarding appropriate subsequent diagnostic steps, should they prove necessary.

**Subsequent Evaluation Steps**

For patients having a “certain diagnosis” after the initial evaluation, no further evaluation is needed. However, the degree of confidence in the diagnosis is very much dependent on individual physician experience, and consequently, many physicians may prefer to undertake one or two selected confirmatory tests before feeling entirely comfortable with moving on to the treatment plan.

For patients having a “suspected diagnosis,” clues from the medical history, physical examination, ECG, and echocardiogram are used to divide patients into those more likely to have a cardiac cause of syncope (i.e., evidence of structural heart disease), or those in whom a neurally mediated reflex cause or orthostatic hypotensive cause (including autonomic dysfunction) is more likely (i.e., patients without evidence of structural cardiac or cardiovascular disease). The strategy for subsequent assessment of patients in whom the initial evaluation fails to provide any plausible diagnostic explanation also varies according to the severity and frequency of the syncope episodes, the occurrence of physical injury, and the potential impact on employment or avocations.1,25

**No Structural Heart Disease**

In the absence of structural heart disease (including a normal ECG), syncope is most often of neurally mediated reflex origin or orthostatic hypotension. As a rule, reflex etiologies predominate in younger patients, and orthostatic causes are more common in older individuals, but the overlap is substantial. However, paroxysmal tachycardias may occur (primarily supraventricular) and cause fainty. Additionally, if the history suggests very frequent apparent “TLOC” spells (i.e., many times per day or per week), “pseudo-syncpe” due to psychiatric disease must be considered.

**Neurally Mediated Reflex Syncope**

For patients in whom neurally mediated reflex syncope seems most likely (based, for example, on medical history and absence of structural heart disease), confirmatory tests may include tilt

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**Evaluation of these patients is recommended when syncope has been recurrent, or has caused injury, accidents, or impairs job safety or performance. Testing primarily consists of tilt-table testing and carotid massage, although electrophysiological (EP) testing may be essential in those cases in which medical history, ECG, or cardiac monitoring findings suggest paroxysmal tachycardias.1**

Ambulatory ECG (AECG) monitoring often plays an important role in the diagnostic evaluation of these patients. However, conventional Holter-type recordings are rarely helpful due to the short recording time. Longer-term “event” recorders offer much greater value. Additionally, recently introduced mobile outpatient cardiac telemetry is becoming increasingly available in the United States, and offers an easy and potentially cost-effective approach for outpatient ECG monitoring.32

As demonstrated in the International Study of Syncope of Uncertain Etiology trial, an ILR can be a very valuable diagnostic aid even early in the diagnostic evaluation of syncope patients.36 In this trial, an ILR was implanted in 82 patients who had no evidence of structural heart disease, and who had a normal ECG and negative tilt-table testing (isolated syncope). In the follow-up period of 3 to 15 months, syncope recurred in 28 patients (34%) and a bradycardic episode suggestive of neurally mediated syncope was recorded in 54% of these cases. The remaining patients had normal sinus rhythm or sinus tachycardia.

Among suspected neurally mediated syncope patients in whom the diagnosis cannot be readily confirmed, the so-called “ATP test” may be of value; but while used in Europe, is currently restricted to clinical investigation in the United States. ATP can provoke a short cardio-inhibitory response of vagal origin.26,27 In patients with unexplained syncope who have definite clinical symptoms, it appears to be useful to detect older patients who are prone to AV block and who may benefit from cardiac pacing. For this test, a rapid injection of 20 mg bolus of ATP is performed during ECG monitoring. Asystole lasting more than 6 seconds, or AV block lasting more than 10 seconds is considered abnormal.

In summary, it is currently believed that the majority of patients with single or infrequent syncope episodes in the absence of identifiable
structural heart disease probably have neurally mediated reflex syncope. However, a certain number of these patients are more likely to have experienced hypotension on an orthostatic basis, especially if they are being treated with diuretic or vasodilator drugs. In some of these cases, the problem may be a primary autonomic disturbance and the prognosis may be poor with progressive slow deterioration. For patients with signs of autonomic failure or neurologic disease, a neurological consultation is necessary, and specific neurological diagnosis should be established.

Autonomic Dysfunction

There are three principal groups of autonomic failure to be considered as part of the TLOC/syncope assessment.

(i) Primary autonomic failure encompasses degenerative diseases, such as multiple system atrophy, pure autonomic failure, and autonomic failure in the context of Parkinson’s disease. Whether less severely disabling conditions such as “postural orthostatic tachycardia syndrome” (a rare cause of frank syncope) should be included among these primary autonomic disorders remains undecided, and will not be considered further here.

(ii) Secondary autonomic failure concerns damage to the autonomic nervous system in the context of other diseases, such as diabetes, kidney and liver failure, and alcoholism.

(iii) In the third group, autonomic failure occurs as a side-effect of medication. Likely culprits are anti-depressants, anti-hypertensives, anti-anginal drugs, vasodilators, and β-adrenergic receptor blocking drugs. In this drug-induced group, autonomic failure is “secondary” to the drug effect and is usually limited to the control of blood pressure during standing.

The differential diagnosis of autonomic failure is complex, and establishing the ultimate diagnosis requires considerable expertise. When the more obvious causes, such as diabetes and drug effects have been excluded, an expert opinion should be sought. In this regard, the evaluation of suspected syncope in the setting of primary autonomic failure may benefit from ancillary neurological testing. In such patients, the faint may occur through an orthostatic hypotension mechanism as well as a result of post-exercise hypotension. In autonomic failure, the neurological dysfunction is often not restricted to blood pressure regulation, and so the history-taking should include assessment of sexual function (impotence), sweating (dry skin, sometimes with patches of compensatory hyperhidrosis), bladder function (both incontinence and retention), gastrointestinal function (delayed stomach emptying, constipation, diarrhea), and pupillary function (blurred vision).

Pseudo-Syncope

An additional consideration in patients without structural heart disease, with a normal ECG, and with many reported “faints,” is psychiatric illness. Psychiatric assessment is especially recommended for patients with very frequent “syncope” (actually pseudo-syncope) recurrences. The latter is particularly warranted if, in addition to complaints of “syncope,” the affected individual appears to be exhibiting other somatic complaints, anxiety, and possibly other psychiatric disorders. Video-EEG monitoring may be helpful for assessing these individuals.

“Drop attacks” may be considered as “pseudo-syncope,” as true loss of consciousness does not occur, but witnesses may easily be misled to believe it has. Cataplexy may similarly prove to be a difficult condition to decipher, and neurological consultation will be essential.

Structural Cardiac Disease Present

For patients with known structural heart disease, selection of testing depends importantly on the severity of underlying cardiac disease. The risk of life-threatening arrhythmias increases as left ventricular function worsens, or conduction system disease becomes more severe, or certain “channelopathies” are identified (e.g., long-QT syndrome, Brugada syndrome). Thus, depending upon individual circumstances, prolonged outpatient AECG monitoring, exercise stress testing, or EP study may be chosen. Apart from the prognostic importance of the presence of heart disease, its absence excludes a cardiac cause of syncope with very few exceptions. In a recent study, heart disease has been shown to be an independent predictor of cardiac cause of syncope, with an approximate sensitivity of 95% and a specificity of 45%; by contrast, the absence of heart disease allowed exclusion of a cardiac cause of syncope in 97% of patients.

In patients with structural heart disease or who have an abnormal ECG, cardiac evaluation consisting of echocardiography, stress testing, and tests for arrhythmia detection such as prolonged AECG monitoring (including use of implantable loop recorders, ILRs) and/or EP study are available, but should be selected based on clinical suspicion of being helpful. Routine “screening” is rarely effective.

AECG monitoring, including conventional wearable “event” recorders, internet-based MCOT and ILR monitoring are widely available for use in the outpatient evaluation of syncope patients, and should be among the first tools used. In patients with exercise-induced syncope, or in whom chest pain suggestive of
ischemia is reported before or after loss of consciousness, stress testing and/or stress imaging are recommended.

In contrast to the forms of AECG noted above, conventional Holter-monitoring (24- or 48-hour recordings) is rarely useful in syncope patients unless the frequency of events is very high (in which situation, a case can be made for in-hospital evaluation). In the more usual circumstance in which patients have only infrequent symptoms, an ILR is likely to be the most effective tool. In fact, it is argued that because they are so cost-effective (on a cost per diagnosis basis as discussed earlier), ILRs may also be indicated at a much earlier stage of the assessment.

Electrophysiologic study (EPS) with programmed electrical stimulation has proven to be a helpful diagnostic test for patients with unexplained syncope who have coronary artery disease. Its utility is more questionable for patients with non-ischemic dilated cardiomyopathy or valvular heart disease. EPS is of little diagnostic value in patients with normal hearts in the absence of documented (or at least strongly suspected) supraventricular or ventricular tachyarrhythmias.1,37–39

In selected patients, EPS may be helpful in defining the presence of sinus node dysfunction, the nature and severity of an AV conduction disturbance, and the nature of an inducible tachycardia. In these settings, such testing may help to define useful treatment strategies such as the need for cardiac pacemaker or ICD implantation, and the potential for transcatheter ablation to be of value.39

**When Is Hospitalization Needed for Evaluation of Syncope?**

Syncope itself does not necessarily require in-hospital diagnostic evaluation. On the other hand, there are no convincing data regarding risk of death or injury during the out-of-hospital evaluation of syncope patients.1

The decision to hospitalize a patient with syncope for diagnostic evaluation depends primarily on the immediate perceived mortality risk to the patient should another TLOC event occur. In older individuals, and in some others who may not heed warnings to avoid potentially hazardous activities, a near-term morbidity risk also plays a role (e.g., fracture risk in the elderly, vocational or occupational hazard in others). Additional concerns relate to public well-being. These may become relevant should a non-compliant fainter resume driving an automobile or commercial vehicle, piloting an aircraft, or persisting with an occupation or avocation, the performance of which might cause risk to others if loss of consciousness were to recur. These latter individuals may need to be removed from such exposure until one is confident that treatment is effective. The duration of that time period must be evaluated on a case-by-case basis; there are no clearcut rules that apply universally. In the case of drivers, the U.S. Department of Transportation website offers some leads regarding qualifications for return to work. An HRS/AHA document is also available on the HRS website, based on a 1996 consensus conference held in Washington DC.40 The Canadian Cardiovascular Society similarly addressed this issue in 2003.41 In regard to commercial airmen, U.S. and European re-qualification can be a very difficult and uncertain process.

**Syncope Management Units**

Many factors may contribute to the effectiveness and expense of the syncope evaluation. However, among the most important of these is the manner in which diagnostic testing and treatment are conducted after individuals present to the emergency department or clinic. The SMU concept entails development of specialized multidisciplinary medical “units” in order to improve the management of these patients.5,11 SMUs operate primarily in the outpatient environment, and bring together a range of pertinent expertise (e.g., cardiology, neurology, geriatrics, psychiatry) in order to address clinical problems in a comprehensive yet cost-effective manner. By way of example, Kenny and colleagues demonstrated the feasibility of saving more than US$4 million in 1 year alone at a single UK hospital due to more efficient management of syncope and “falls” patients.5 The economic benefit arose in large measure from reduced readmission rates, and marked reduction of hospital in-patient days. Similar benefits may be achievable in North America.42 ESC syncope guidelines1 encourage broader application of the SMU concept, and European medical centers are taking the lead in this regard. In North America, the SMU concept has yet to become a standard strategy, but may become more common as the medical and economic benefits become more apparent.

**Conclusions**

Syncope is one form of TLOC, and distinguishing true syncope from other types of TLOC is a crucial responsibility for the clinician. Unfortunately, the literature has often been misleading in this regard. The ESC syncope guidelines are clearly the most authoritative source of advice.

Syncope is a relatively common problem faced by medical practitioners in many specialties, and one that causes considerable anxiety for affected individuals and their families. Fortunately, in the majority of patients, the cause of syncope is relatively benign, and a strategy based on patient education and prevention of recurrences is
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sufficient. However, in a few patients (primarily those with structural cardiac disease), syncope portends serious disease and a worrisome prognosis. Differentiating these two groups, and determining the basis for symptoms with sufficient confidence to assess prognosis and initiate effective therapy is the essential management goal. Careful history-taking, a thorough physical examination, and judicious use of tests, will not only increase the diagnostic yield, but will also enhance treatment success and patient safety, and will ultimately reduce overall healthcare costs.

References